

Fischer (L.)

al

CLINICAL EXPERIENCE

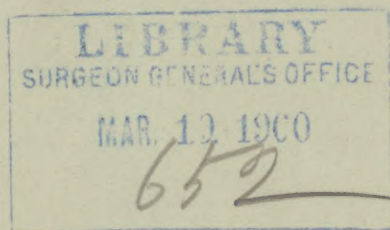
WITH

ANTI-STREPTOCOCCUS SERUM.

presented
BY

LOUIS FISCHER, M.D.,

New York.



CLINICAL EXPERIENCE WITH ANTI-STREPTOCOCCUS SERUM.*

BY LOUIS FISCHER, M.D.

New York.

When the treatment of diphtheria with antitoxin became generalized, great hopes were entertained by the profession upon the announcement of a similar discovery with Marmorek's anti-streptococcus serum.

This announcement came from the Pasteur Institute at Paris. It was first recommended as a specific in the treatment of all diseases caused by the streptococcus, and therefore was urged as a specific in the treatment of scarlet fever. It was furthermore recommended as a specific in erysipelas, and also in the treatment of puerperal septicæmia. In fact, all septic conditions caused by *post-mortem* wounds were to be similarly treated. Thus, we have had occasion to see what this serum can accomplish.

My first experience with this Marmorek's serum I owe to the courtesy of Prof. A. Baginsky. It was in the summer of 1896 that I watched with great interest a series of cases of scarlet fever treated by the anti-streptococcus serum in the Scarlet Fever Pavilion, which is part of the Kaiser and Kaiser Frederick Children's Hospital at Berlin.

The treatment pursued consisted in subjecting a series of cases of mild, severe, and malignant scarlet fever to the therapeutic influence of this serum, and by noting the results night and day. Owing to the large number of assistants at the disposal of Prof. Baginsky, in addition to the laboratory facilities, all details were handled in a masterly manner. Some cases received injections of 10-20, and some as much as 70-80 c.c. during each treatment.

Recognizing the value of Prof. Baginsky's advice in the treatment of diphtheria, I naturally was anxious to note his results in the treatment by this new therapeutic agent. He cautioned me not to use the serum for the present, and said to me that it is not a specific in the treatment of scarlet fever, in the sense that antitoxin is advised in the specific treatment of diphtheria.

In his text-book on Diseases of Children, fifth edition, published in Berlin, 1896, in his article on scarlet fever, page 151,

*Read before the Section on Pediatrics, New York Academy of Medicine, May 12, 1898.

speaking of Marmorek's anti-streptococcus serum, he distinctly says that "he believes that it does no harm."

This is now the second year since I have tried the value of this anti-streptococcus serum in various diseases.

SCARLET FEVER.—A. Z., three and a half years of age, had been sick with scarlet fever for about one week, when we took charge of the case on April 13, 1897. When the child was first seen, it had a temperature of 102.5°; pulse, 140, soft, weak, and intermittent. The mouth and pharynx were filled with dry, greyish, fetid membranes. There was a purulent nasal discharge, an excoriation around the *alæ nasi*, besides a mild bronchitis. The child was extremely constipated, had anorexia, was intensely thirsty. There had been a history of previous vomiting. The child was extremely restless, and the face showed a decided condition of sepsis, being pale, eyes sunken, nose pointed, furrows round the eyes deeply marked, and a sickening odor emanated from the child's body. The child was put on calomel powders, which produced some very vile-smelling evacuations. Large quantities of brandy and milk and seltzer were also given, and diffusible stimulants, like carbonate of ammonia, were ordered. As the temperature rose, and there was evidence of delirium, cooling baths were ordered, which seemed to have a tonic effect.

On the 17th, the child received an injection of 10 c.c. of anti-streptococcus serum, and noticing no distinct change in the child's condition, the same dose was repeated on the 24th. The child showed no signs of improvement; the temperature was somewhat reduced, but the general condition was certainly not improved.

On the 30th, *exitus lethalis*.

The above case was attended by Emil Joel, M.D., from whom I received the above report, and was seen by me several times with him.

Another equally interesting case is the following:

C. G., female, six years old, and seen by me on October 17, 1897. The mother told me that the child had been vomiting, and it had some diarrhoea, the latter caused by a cathartic that she had given. The child was covered with a rash, but had, according to the mother's history, been well until yesterday. She complained of headache and slight pain in the throat. Inquiry elicited the fact that a child in the same house had had scarlet fever several weeks ago, and that this patient under consideration had been exposed before the character of the disease was defined. Physical examination showed a poor-nourished child, pigeon-breasted, rachitic head and limbs, an otitis purulenta dextra, which the mother told me had existed for the last year since the child's attack of measles. The eruption covered

the chest and limbs, and was not plain on the back nor on the face. The pharynx and fauces were congested, but showed no patches; the tongue was slightly coated, but did not show the characteristic strawberry appearance usually found in these cases. The temperature was 104° in the rectum at 9 A.M.; pulse, 138. The urine, according to the mother's history, was passed freely. The diagnosis of scarlet fever had been made.

I requested permission to use the anti-streptococcus serum. The child received 10 c.c. on the evening of the same day, which was injected subcutaneously between the shoulder blades about 5 P.M. The temperature at the time of the injection was 105.2° in the rectum; pulse, 156. At 9 P.M. the temperature was 105° in the rectum; pulse, 150. The child was still nauseated and intensely thirsty.

The following morning, at 9 A.M. (October 18th), the temperature was 104° ; pulse, 124; general condition the same, with the exception of diarrhœa, which had subsided, the child having been put on a rice, barley, and white of egg diet; no stimulants had been given. On the evening of the same day, at 6 P.M., the temperature rose to 104.8° ; pulse 146; no delirium; no evidence of sepsis.

October 19th, 9 A.M., the child's condition seemed the same; eruption was more defined, covering the face, back, extremities, and abdomen. The temperature in the evening again rose to 104.6° .

October 20th, the child's condition is bright; temperature, 103.4° ; pulse, 124; the throat intensely congested; two small necrotic patches can be seen on the left tonsil, a culture on blood serum showed staphylococci and streptococci.

October 21st, 9 A.M., the temperature being still 102.6° , another injection of 10 c.c. of serum was given. I left my thermometer with instructions to take temperature. Two hours later (at 11 A.M.), I saw her; the temperature remained 102.6° . On the evening of the same day, I saw the child again, the temperature was 104° ; pulse, 134.

October 22d, temperature in the morning, 101.3° ; pulse, 118; 6 P.M., same day, temperature was 102.6° ; pulse, 102.

October 23d, temperature 9 A.M., 101° ; pulse, 98; 6 P.M., 100.6° ; pulse, 90.

October 24th, 9 A.M., temperature, 100.4° ; pulse, 94; 6 P.M., 99.4° ; pulse, 96.

THE ERUPTION.—During the course of the disease, the eruption seemed to gradually spread, and remained at its height covering the whole body for three days, from the 19th until the 22d. It then began to fade, and on the 25th appeared like small erythematous patches scattered over isolated areas of the body. It seemed to me that in this case the eruption was not influenced by the injections used. The urine showed slight traces of albumen during the first week of the disease. During the second

week the urine contained two pro mille of albumen, but showed no casts.

The child desquamated profusely; post-scarlatinal nephritis continued for some time, with œdema of face, feet, and hands. The urine was not very scanty, however.

The child received some iron and decoction of cinchona bark, and made an uneventful recovery.

In the London *Lancet*, March 19, 1896, Harold Low reports a case of scarlet fever complicated with acute suppurative otitis media, and acute hemorrhagic septicemia treated by anti-streptococcus serum.

Low reports a case of scarlet fever in which, on the fourth day, pain in the ear developed, followed within twenty-four hours by a discharge. Two days later there was evidence of mastoid suppuration, and when the antrum was opened a considerable amount of pus was discharged. This was followed by drowsiness, irregular temperature, and some jaundice. A diagnosis of septicemia was made, and injections of anti-streptococcus serum were at once commenced. The patient's condition for a time grew worse, then improved, the jaundice disappeared, and finally recovery ensued. Before this was complete, however, the patient had several attacks of epistaxis and a severe purpuric eruption. A bouillon-culture of the blood, made before the commencement of the treatment, showed the presence of the streptococcus. Altogether 263 c.c. of serum were used.

In a series of fifty-seven cases published by Prof. A. Baginsky, in the Berlin *Clin. Weekly* of 1896, No. 16, nine cases must be excluded, as the treatment was not satisfactory, having been discontinued or otherwise; the other forty-eight cases are divided into several groups.

In twenty-seven of these cases, the result was an exceptionally good one. In these twenty-seven there were no complications encountered. In four of these latter cases, after the injections of the serum, there appeared a mild form of nephritis. In another case a suppurating form of otitis, and two other cases showed a severe angina, and a severe painful glandular swelling.

A point worth noting was the fact that after the injections, and within the next two or three days following, the temperature was suddenly reduced. The angina encountered terminated favorably in all of his series.

Albuminuria was met but rarely, and in only one case could nephritis be suspected.

The author warns against accepting too hasty deductions from his reported experiences with severe forms of nephritis, because he has found that these latter conditions occur less often in hospital practice than in his private cases. This he attributes to a strict milk diet, and better hygienic conditions.

In another group of seven cases, the author reports the lethal ending of the same, owing to various complications. The author believes that the serum might have been used in a much larger dose, and that possibly some benefit could have been deprived from the same.

In another series of cases, in spite of a large number of injections, and a sufficient quantity of the same, there was no appreciable benefit, although all cases recovered.

In the other seven cases, severe complications ensued, and the author believes he did not have enough of the remedy to give it in proper doses.

In five other cases, the serum was used to modify special complications. In one of these cases it did not seem to have any influence, and the child died. The four others recovered.

The mortality was 14.6 per cent. The mortality in the hospital has ranged in the last year from 22.6 per cent. to 34.3 per cent.

The author refers to the fact that the scarlet fever mortality is subject to periodical changes, and, therefore, does not show positive deductions to be drawn from the above quoted figures.

He does not, however, find the course of children treated with serum any worse than otherwise. The after-affects were in no wise different from those noticed during the treatment of diphtheria with antitoxin. He still continues the use of the same Marmorek's serum.

In the *Medical Record*, March 14, 1896, Dr. Berg, speaking of the treatment of pneumonia as a complication of diphtheria, describes at length the anti-streptococcus serum, and its application to the various diseases known to be caused by these micro-organisms.

Dr. Alexander Marmorek (*Annales de Pasteur*, July, 1895), states the belief that different forms of streptococci are varieties of a single microbe. Thus, Marmorek believes that Fehleisen's erysipelas streptococcus cannot only produce erysipelas, but

when sufficiently virulent, can produce meningitis, pneumonia, abscess, septicæmia. It certainly depends upon the point of entry into the body, as to what disease shall be produced, plus the degree of virulence contained in this streptococcus.

Berg, describing the method of producing the anti-streptococcus serum, states that the ideal serum will be that obtained from animals immunized against streptococci infinitely more virulent than any to the action of which man can by any possibility become subject.

We have thus far succeeded in producing an anti-streptococcus serum, but not a streptococcus antitoxin, the animals having been immunized against the streptococcus germ, and not against the toxin produced by the streptococcus.

The attempt has been made to immunize horses to the toxin produced by the streptococcus, but it is very difficult to obtain a toxin sufficiently virulent to be of any use in immunizing horses.

At the time of publishing his article, Berg stated that the New York Health Department was engaged in the production of an anti-streptococcus serum, and does not, therefore, report any clinical results with the same. I have learned, however, that since that time, Dr. J. Winters Brannan and Dr. Berg have used this serum at the Willard Parker Hospital.

The following three cases I owe to the courtesy of Dr. Sig. Cohn, the first of which I had the pleasure of seeing with him once.

A child, Rosy, four years old, was sick three to four days prior to Dr. Cohn's first visit. When he first examined the child he found a decided case of scarlet fever and angina necrotica.

Culture from this case sent to the New York Health Department showed K.L.B. and streptococci. At the request of Dr. Cohn, the Inspector of the Health Department injected the child with antitoxin; quantity unknown.

The temperature ranged from 104° to 105° . The throat symptoms increased, and as the child's general condition did not improve, the doctor decided to try an injection of 10 c.c. of anti-streptococcus serum.

At this time I saw the child with Dr. Cohn. We secured a nurse, and irrigated the nose with a solution of boracic acid. The child's temperature went down to 101° between two to three days after the injection of anti-streptococcus serum. Several days later the child again grew worse, the temperature

went higher, and Dr. Cohn gave another injection of 8 c.c. of anti-streptococcus serum. This was followed by no improvement.

After the scarlatinal eruption faded, a new eruption resembling measles, appeared three days following the second injection of anti-streptococcus serum. The urine, which was carefully examined, did not show any traces of albumen nor casts. The child died of heart failure and collapse.

The second child in this family was five years old; showed an eruption of scarlet fever and angina necrotica, also received an injection from the New York Health Department of diphtheria antitoxin. As there was no improvement following this injection, the child was also injected with 10 c.c. of Marmorek's anti-streptococcus serum. This was followed by no reaction, nor any decided improvement directly attributable to the serum. This child recovered.

The third child, a baby one year old, had a very mild scarlatinal eruption; did not show any angina. In fact, the throat appeared normal. This child was not injected with anti-streptococcus serum, and the case recovered very easily with no complications, and no sequela. These children were attended about three months ago.

A case of erysipelas attended by Dr. Sig. Cohn, and which was not seen by me, was between three to four years old. It was sick but a short time before the doctor's first visit. The little patient had a typical erysipelas flush on the lower extremities; this gradually extended to the abdomen, and then to the back. The doctor used lead and opium wash externally, followed later by an ointment of ichthyol. Not finding any improvement, and finding that the erysipelas had spread alarmingly, the temperature at this time being 104°, the doctor injected at 6 P.M., 8 c.c. of anti-streptococcus serum.

The following morning the temperature was normal; the erysipelas faded and gradually subsided. No other treatment was used, and the child recovered very rapidly.

Schenk (*Central Blatt für Bacteriologie*, page 170, Band xxiii., Part III.), treated in the State Institute, and reported in the *Vienna Klin. Wochen*, 28th of October, 1898, four animals (three horses and one mule), according to Marmorek. They received increased doses of streptococcus serum. The animals had previously received injections of diphtheria toxin. The animals all tolerated the poison well, and were able to withstand the poisonous effects of living cultures.

One animal withstood 200 c.c. without any after-effects. After ten months' treatment, the serum of these animals was tested for their therapeutic value.

Sixty rabbits were injected with 0.1-5 c.c.m., and twenty hours later injected with one hundred times the usual poisonous dose of toxin.

Although the animals so previously injected showed a similar mortality, 36 per cent. against 11 per cent. of controlled animals, still this author could not arrive at any positive deductions from the amount of poison injected or the amount of prophylactic serum used to control or neutralize the poison.

His results are the same as those of Petruschky, and questions the value of the serum made according to the method of Marmorek. Still poorer were the healing results with this same serum, for out of twenty-one rabbits thus treated, nineteen died.

The following case of a baby, K., one year old, female, was feverish and restless for about two days, when Dr. Aronson was called. According to the family the doctor did not make a diagnosis, as the disease was not properly developed.

On the third day of the child's illness, Dr. Berger was called and diagnosed the case as erysipelas. On the fourth day of the disease the child grew worse. The disease spread very rapidly, and there was a marked rise in the temperature. The doctor had used ichthyol ointment locally with no apparent benefit.

On the fifth day of the child's illness, Dr. Henry M. Groehl was called in, and found a very well marked case of erysipelas, involving the both lower extremities, and spread from there to the back, covering the same, and over the abdomen. The temperature at the time of his first visit was 104.2°; the child was very restless. He ordered locally lead and opium wash to cool the surface, and internally he gave calomel and phenacetine with sparteine.

The following day, the sixth day of the child's illness, Dr. Groehl found the child much improved. The mother stated that it had rested well; the child would sit up and play. The temperature had fallen to 99°; the pulse was good.

The erysipelas flush was not spreading; the color was not so red, and some areas of the skin had lost the hard and elevated thickened induration. The child was in every way greatly improved, and was nursed by its mother, taking the breast with evident relish.

The seventh day of the child's illness, there was a marked change for the worse. The temperature still remaining at 99°; the pulse was rapid and feeble; there was continuous vomiting. The inflammation had suddenly spread from the abdomen to the chest, almost completely covering the child. The child's appearance was decidedly septic. The child vomited long after all

drinks; the mouth had been stopped. In fact, long after rectal feeding had been commenced, the vomiting persisted.

On the eighth day of the child's illness, Dr. Louis Fischer was called in consultation, and after going over the history of the case and the treatment pursued, recommended injections of 10 c.c. of anti-streptococcus serum. This was injected in the usual aseptic manner, just as we inject antitoxin, on the morning of the eighth day of the child's illness. On the evening of the same day that the injection was given there was no reaction. The child continued the same.

The following day, about three hours before the *exitus letalis*, the body was covered with ecchymotic spots. The various parts of the body were covered with discolorations; some of them resembled the colors of the rainbow.

Two very instructive cases are the following:

A child seven years old, complained of nausea and vomiting quite freely. The mother, believing the child had a disordered stomach, gave her some citrate of magnesia, which had quite a marked laxative effect.

The following day the child complained of intense headache, and being very feverish and thirsty, was put to bed, and a physician sent for. On examining the child he found the body covered with a distinct scarlatinal eruption. He ordered spir. mindereri; a teaspoonful every two hours, and a liquid diet. The next day he injected 10 c.c. of anti-streptococcus serum. The temperature was between 103° and 104° ; the exact measurement not noted.

The next day, finding the child's headache still persisted, and the general condition not improved, he again injected 10 c.c., and continued to inject every day for seven successive days 10 c.c., until 70 c.c. had been used.

The temperature ranged from 105° to 106° in the evening during the second week of the child's illness, and from 103° to 104° every morning.

When I saw the child, at the request of the family, I found a condition of general furunculosis on the back, and in the axillæ on the shoulders, over the left patella. The family objected most strenuously to incising the furunculosis, and thus these furuncles were allowed to open spontaneously.

The urine was very turbid, high colored and loaded with albumen. On boiling the same it almost coagulated in the test tubes. There were also casts found on microscopic examination. The child suffered from a continuous diarrhœa, which bismuth and injections of laudanum with starch would not control. The throat showed small areas of necrotic scarlatinal pseudo membrane, and there was quite some discharge from the nose. There was also a purulent ophthalmia, the eyes being glued together when the child dozed. There was a constant stupor,

and the child seemed to be drowsy. The nose was pinched; there was an intense thirst all the time, and continuous cough, which had appeared when I first saw the child, and which we first thought resembled pertussis, proved later, on careful physical examination to be an empyema. The child died in a condition of most profound sepsis several days after the aspiration of the purulent effusion.

The family objected to the operation of empyema. During the course of this child's treatment, an older child (nine years) which had been exposed and was now isolated, contracted the disease, the mother calling our attention to the persistent vomiting and sore throat. In this case I used quite some diplomacy in order to convince the attendant that I did not believe anti-streptococcus serum could do any good. In fact I advised him that if he would again inject the second child, that I would withdraw from the case. As the family insisted on my continuing to attend the child with the attending physician, we used carbolated vaseline inunction, and the usual expectant plan of treatment, treating symptoms as they arose, giving an iron and glycerine gargle, and although this child suffered with a nephritis for six weeks, it made an uneventful recovery.

In an elaborate paper on pneumonia complicating diphtheria, H. W. Berg (*Medical Record*, March 14, 1896), suggests the practicability of using anti-streptococcus serum in this disease.

W. H. Park (The W. M. Carpenter Lecture, 1897), states that the rapid deterioration of serum in vials may account for the absence of curative powers in the serum. He further says, that the preparations of anti-streptococcus serum now on the market are either quite weak or entirely wanting in curative substances.

Van de Belde, (*Pediatrics*, Vol. 4, Nos. 9 and 10, 1897, *Arch. de Med. Exper.*) studied the question as to the protective value of the anti-streptococcus serum prepared from one variety of streptococcus, and to see whether it was equally protective against other streptococci. Selecting two varieties, one obtained from a sore throat, the other from a case of puerperal septicæmia, he tested the effects of their respective sera. His conclusions were, that the serum of one variety was only curative against that same variety of streptococcus. Thus, a serum made from a streptococcus in puerperal septicæmia was only protective against this same disease.

Steele (*British Med. Journal*, Oct. 3, 1897), reports twenty-six cases of puerperal septicæmia where serum was used. There were sixteen recoveries; ten died. He says there are so many other causes for transitory rise of temperature during the

Pages 11-12 missing

FROM
ARCHIVES
OF
PEDIATRICS

A MONTHLY JOURNAL DEVOTED TO DISEASES OF
INFANTS AND CHILDREN.

EDITED BY

FLOYD M. CRANDALL, M.D.

“Pediatrics is the specialty of the
general practitioner.”

Volume begins with January. Sub-
scriptions may begin at any time.
\$3.00 a year in advance.

E. B. TREAT & CO., Publishers,
241-243 West 23d Street, New York.

